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TITLE: Cost-Effective Magnetoencephalography Based on Time-Encoded Optical Fiber Interferometry for Epilepsy and Tinnitus Diagnosis

PRINCIPAL INVESTIGATOR: Jing Xia

CONTRACTING ORGANIZATION: University of California
Irvine, CA 92617

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6. AUTHOR(S)
Jing Xia

E-Mail: xia.jing@uci.edu

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

UNIVERSITY OF CALIFORNIA, IRVINE NANCY LEWIS 5171 CALIFORNIA AVE STE 150
IRVINE CA 92617-3067

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13. SUPPLEMENTARY NOTES

14. ABSTRACT
Functional neuroimaging is critical to the understanding and diagnosis of neurological disorders especially Epilepsy and Tinnitus. Both conditions severely harm servicemen and veterans' wellbeing and combat capability, but are difficult to diagnose with anatomical imaging tools like MRI and CT due to the functional nature of these disorders. In contrast Magnetoencephalography (MEG), which spatially monitors brain activities in real time has been proven effective at studying, screening and diagnosing Epilepsy and Tinnitus, providing insightful information for surgical treatments. The proposed MEG technique is based on two major innovations, whose feasibility will be tested in this project. (I) Interferometric magnetic detection: A Sagnac fiber interferometer will be constructed and used to perform magnetic sensing by measuring the magnetic-field-induced optical phase shift in optically pumped Rubidium (Rb) vapor placed outside patient's head. This interferometric technique is expected to be more sensitive than existing atomic magnetometers.

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INTRODUCTION:

Functional neuroimaging is critical to the understanding and diagnosis of neurological disorders especially Epilepsy and Tinnitus. Both conditions severely harm servicemen and veterans' wellbeing and combat capability, but are difficult to diagnose with anatomical imaging tools like MRI and CT due to the functional nature of these disorders. In contrast Magnetoencephalography (MEG), which spatially monitors brain activities in real time has been proven effective at studying, screening and diagnosing Epilepsy and Tinnitus, providing insightful information for surgical treatments. However, the high acquisition ($3 million) and operational ($200 K per year) costs severely limits the availability of MEG in VA medical centers. The high costs intrinsically originate from (1) the use of low temperature superconducting interference devices (SQUID) magnetic sensors and/or (2) simultaneous use of hundreds of sensors in a MEG machine. In this project, we aim to develop a novel MEG technique, which uses a single non-cryogenic sensor to perform high speed MEG diagnosis, significantly reducing the cost and enhancing the performance. The proposed MEG technique is based on two major innovations, whose feasibility will be tested in this project. (I) Interferometric magnetic detection: A Sagnac fiber interferometer will be constructed and used to perform magnetic sensing by measuring the magnetic-field-induced optical phase shift in optically pumped Rubidium (Rb) vapor placed outside patient's head. This interferometric technique is expected to be more sensitive than existing atomic magnetometers, even surpassing that of SQUID. A successful experiment would be a major progress in MEG research itself. (II) Wavelength-encoded MEG imaging using a single fiber sensor: This reduces the price of the whole MEG machine to that of a single fiber sensor. A 2D optical disperser will be used to project different wavelengths of light from an interferometer onto different locations in a MEG helmet consisting of a layer of Rb vapor. The inference light contains both the magnetic information and location information in the forms of optical intensity and wavelength respectively. A length of dispersive fiber and a computer are used to first "decode" the optical interference signal into dispersed optical wave-packet and then reconstruct MEG images, all in real-time. Based on simultaneous studies of Sagnac MEG, EEG and fMRI, we seek to develop a pattern-recognition based algorithm for detecting and locating brain anomalies. This fast algorithm bypasses the need for the difficult solution of "biomagnetic inverse problem" and is potentially helpful for early screening of epilepsy and tinnitus. Success of this project would

make possible a novel MEG technique where the performance is enhanced 10 fold and the cost is reduced 30 times. This would make a qualitative change to the availabilities of MEG. It also has other virtues including compact size (size of a football helmet), high speed (up to 1 million images per second) and the patient can move freely as he/she is linked through a single fiber to MEG instrument. The compact size opens the possibility of deploying MEG to field hospitals and battleships where servicemen who have been subject to TBI and extreme noise could be screened for functional brain disorders before Epilepsy and Tinnitus fully develop. It is possible to envision future high speed MEG studies of Epilepsy and Tinnitus in environments simulating that of battlefield where patients cab move freely. This will help to find ways to prevent Epilepsy and Tinnitus in servicemen and veterans.

KEYWORDS: *Sagnac, MEG, Magnetometer, Imaging.*

ACCOMPLISHMENTS:

What were the major goals of the project?

Task I. A fiber-interferometer setup will be constructed to perform accurate magnetic field sensing. (6 months).

The interferometer was constructed by July 2015.

Taks II. Simultaneous 2D MEG image with a single fiber interferometer (6 months).

This task is not completed. Due to unforeseen difficulties such as instability of pump laser, fluctuations in the environmental magnetic field, this task is not completed at the end date of this grant. The PI is still fighting these problems today. It seems that a more advanced laser source is required to solve the problem of unstable laser wavelength. And a mu-metal based magnetic field shield room is needed to reduce the environmental magnetic field to a level acceptable for MEG detection. Such a mu-metal room is required for commercial MEG systems and would cost $ 1M, which is beyond the budget of this project.

Taks III. Anomaly pattern recognition algorithm, with accompanying EEG and fMRI studies (6 months).

This task is based on the completion of task II, and hence is not performed.

What was accomplished under these goals?

1) <u>major activities</u>

We have constructed a fiber optical Sagnac interferometer, that for the first time is coupled to a Rb vapor cell. The demonstrated Faraday sensitivity was 5 nano-radian over hours of operation time, which is the new record for Faraday measurements.

2) <u>specific objectives</u>

AIM I. High-speed MEG imaging with a single fiber Sagnac sensor

AIM II. Development and testing of fast recognition algorithm with accompanying EEG and fMRI studies

3) <u>significant results or key outcomes</u>

Demonstration of a Sagnac fiber interferometer with 5 nrad Faraday resolution

A schematic of the Sagnac interferometer used in this experiment is shown in the figure below.

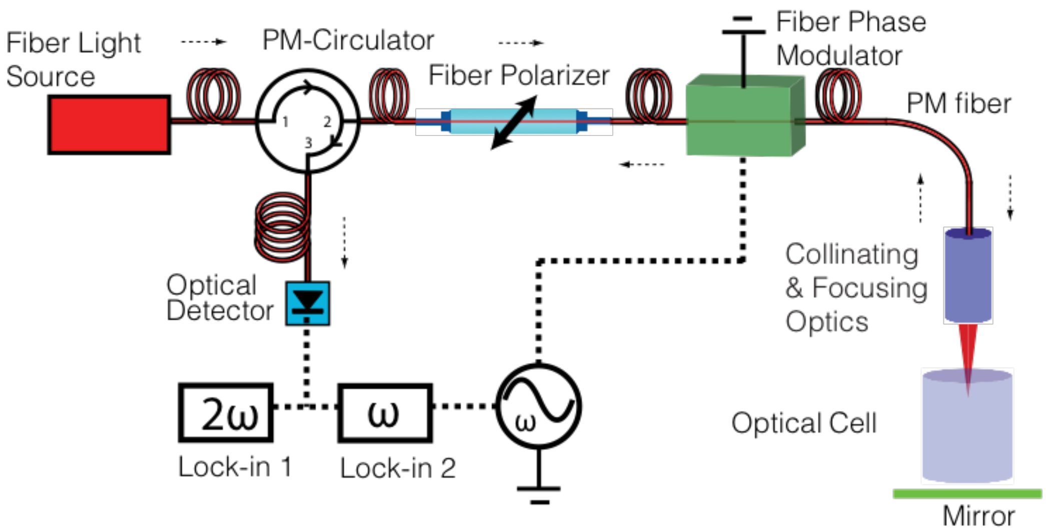

Figure 1 Schematic of Sagnac interferometer. The Faraday signal is measured using a Sagnac interferometer. Two orthogonal polarizations of light a phase-shift modulated and reflected from the surface of the sample after passing through a quarter-wave plate.

In a fiber-optic Sagnac interferometer, light from a laser source passes through a polarization maintaining (PM) circulator and is polarized. A half-wave plate is then used to rotate the polarization axis to 45 degrees with respect to the axis of a phase shift modulator. This modulator adds a time-varying phase shift to the light. However, the amplitude of the phase shift and the optical path length are different for the in-plane and out-of-plane polarizations of light. After passing through the modulator, the in-plane and out-of-plane polarizations are no longer coherent with each other, and each polarization beam has a time varying phase shift of different amplitude. The light is then routed via a PM fiber to optics mounted on a stage capable of sub-micron step size in both the x- and y-directions. After exiting the PM fiber, the light is passed through a quarter-wave plate which converts the orthogonal, linear polarizations into left- and right-circular polarizations. Finally, it is focused onto the vapor cell, which contains optical viewports

on each face allowing the light to pass from the focusing element to the vapor. Upon reflection from the rear face, there is a phase shift between the two polarizations equal to the twice the Faraday signal. After passing through the quarter-wave plate the polarization axis of the two beams had been swapped. On the return trip each beam travels through the system with a polarization orthogonal to that of its outgoing trip. The net result is that each beam travels along the exact same optical path but in opposite direction over the round trip. Once each beam passes through the phase shift modulator again, the two beams are once again coherent but have phases differences due to the Faraday effect ($2\theta_k$) as well as that caused by the phase shift modulation [$\phi_m(\sin(\omega_m(t + \tau)) - \sin(\omega_m t))$, where ω_m is the modulation frequency and ϕ_m is the difference in amplitudes between the in-plane and out-of-plane modulation]. The two beams interfere, resulting in an elliptically polarized beam, the in-plane component of which is routed to a photo detector. If ω_m is chosen such that $\tau\omega_m = \pi$, lock-in detection can be used to determine θ_k by comparing the detected signal at ω_m and $2\omega_m$.

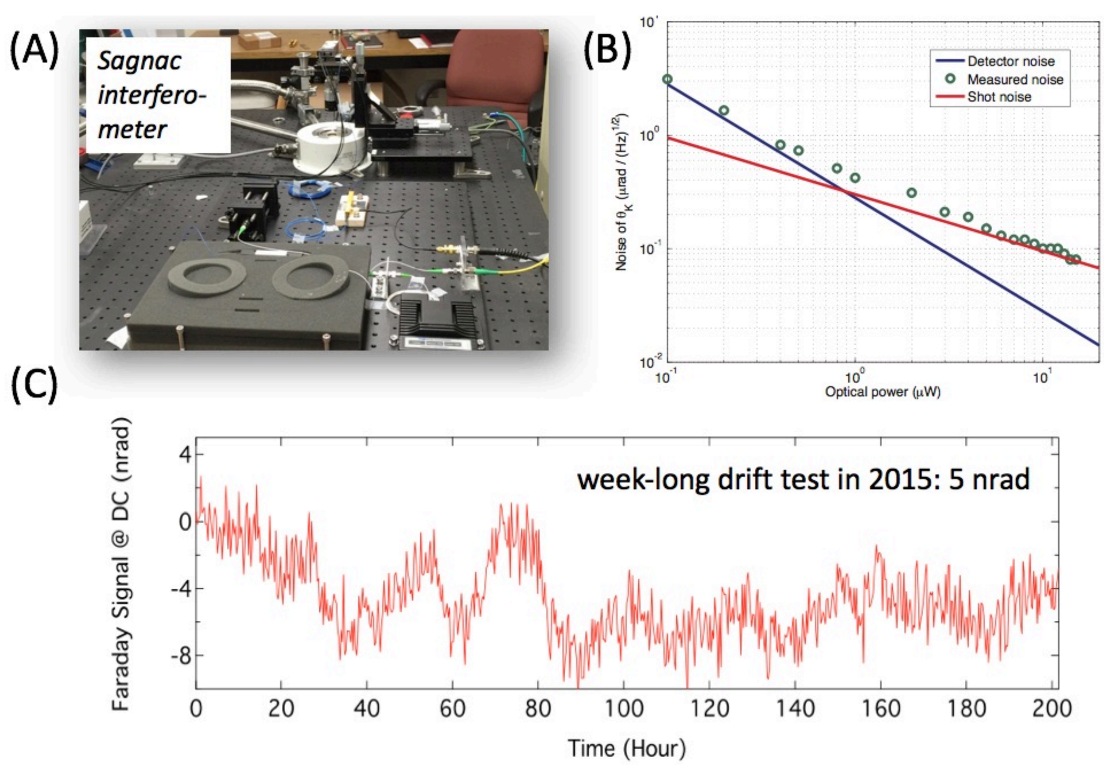

Figure 2 Picture and performance of Sagnac interferometer. (A) Picture of the constructed Sagnac interferometer. (B) Noise as a function of detected optical power in the Sagnac inter- ferrometer. Below 3 μW the apparatus is limited by detector noise. Between 3 μW and 11 μW, the apparatus is photon shot-noise limited. At even higher optical power, other sources of noise may arise. (C) The Faraday resolution is limited by long-term drift to 5×10^{-9} rad, which is a new record.

A picture of the constructed Sagnac interferometer is shown above. The performance was evaluated by measuring its short-term noise level and long term drift. The former determines the required optical power and the latter determines the ultimate Faraday sensitivity.

The measured noise level is shown in panel B. Several sources of noise may be found in a magneto-optic Sagnac interferometer. Amplitude modulation due to back-scattering and improper alignment of the EOM may contribute to both noise and offset. However, this was largely reduced by placing two focusing lenses on each side of the EOM to reduce back scattering from the flat surface of the EOM crystal and by placing the EOM as straight as possible to reduce amplitude modulation. Fluctuations in temperature and fringing magnetic field mostly contribute to offset instead of to noise, since the fluctuations at at a much lower frequency then 3 Mhz used in this setup. For the few μW of optical power used, the major contributions to the noise in the setup are found to be detector noise and photon shot noise. The noise-equivalent-power (NEP) of the New Focus 150 Mhz bandwidth detector used in the experiment is 0.5 pW/√Hz. For the Sagnac interferometer biased to its dark fringe and an average optical power of Pave at the detector, this is equivalent to a Kerr angle noise of 0.28(μrad/√Hz)/P. Photon shot-noise comes from statistical fluctuations in the number of particles received at the detector. For 80% quantum efficiency of the detector, the shot-noise at will be 0.3/ √P (μrad/ Hz). Both detector noise and shot-noise are plotted as a function of Pave in figure 3.15. Experimental noise level was measured by monitoring fluctuations in Kerr readings over several minutes with a dielectric mirror as the sample. The one σ noise level was then calculated from the data. The process was repeated for optical powers at the detector from 0.1 μW to 11 μW. The results are plotted in figure 3.15 for comparison. It can be easily seen that below 3 μW the apparatus is limited by detector noise. Between 3 μW and 11 μW, the apparatus is photon shot-noise limited. However, the apparatus may not be shot-noise limited at even higher optical powers, as other sources of noise may arise. In fact, at optical powers in the mW

range, the fluctuations in the output power of the light source itself may be a major source of error, as seen in many high power optical experiments. Besides, at much higher optical power, the non-linear Kerr effect may no longer be eligible despite the use of low-coherence light sources. These need to be taken into consideration if the Sagnac geometry described in this thesis is going to be scaled up to higher optical powers for other measurements.

The ultimate resolution for quasi-static magneto-optic Faraday measurements (shown in panel C) is not determined by noise, but instead by drift. The experimental data can be averaged over a long time to achieve smaller fluctuations to an extend when drift over the averaging time comes into play. For temperature-dependent measurements, drift over temperature is equally important. Thanks to the elegant reciprocal geometry of the Sagnac interferometer, many sources of drift that would present in other polarimetry techniques were eliminated here. And after proper manufacturing and aligning the optics and electronics, the drift can be reduced to a very low level. We have performed various characterization of the instrument showing even better MOKE sensitivities. For example, a one-week run in 2015 showed the resolution to be 5 nrad as illustrated in the panel C of the above figure. This level of sensitivity is about two times better than previous Sagnac interferometers. And is 2 orders of magnitude better than competing polarimetry-based Faraday techniques.

<u>*Couple a Rb Vapor cell to the Sagnac interferometer*</u>

To perform MEG measurements, a Rb vapor cell needs to be coupled to the above Sagnac interferometer. And a schematics is shown below. The magnetic sensing medium is vapor of alkali atoms (Rb, Cs or K) contained in a glass cell. The spins of alkali atoms are polarized by a circularly polarized pump light tuned to resonance (hence large absorption). If we put the vapor in an external magnetic field that we want to measure, the spins would precess resulting in a component of the spin perpendicular to both the original spin polarization and the external field. If we pass a probe light along that direction, the spin component would yield different optical phase ϕ_L and ϕ_R for left and right circularly polarized light, or commonly referred as the magneto-optic Faraday effect: the rotation (θ_F) of polarization plane of a linearly polarized light. One can show that: $\theta_F = (\phi_L - \phi_R)/2$. *The sensitivity of the magnetometer is determined by several factors* $\delta B = \frac{1}{g\mu_B}\frac{\hbar}{\sqrt{N\tau T}}$ *, where N is alkali atom density, τ is the their coherence time. And T is*

measurement time, μ_B is Bohr magneton, g is the Lande factor and ħ is Planks constant. For better sensitivity, one can use high-density vapor (larger N) and use various techniques to enhance the coherence time T. One way to achieve large T is to reduce the collision with cell walls, either by filling the wall with buffer gas, which ensures that the atoms optically polarized in the central part of the cell take a long time to diffuse to the walls, or by coating the cell wall with a non-relaxing coating, typically paraffin. At high density and small collision rate with the cell wall, the coherence time T becomes dominated by collisions between alkali atoms, mostly through spin-exchange process: interchange of spins between two colliding atoms with the conservation of total spin.

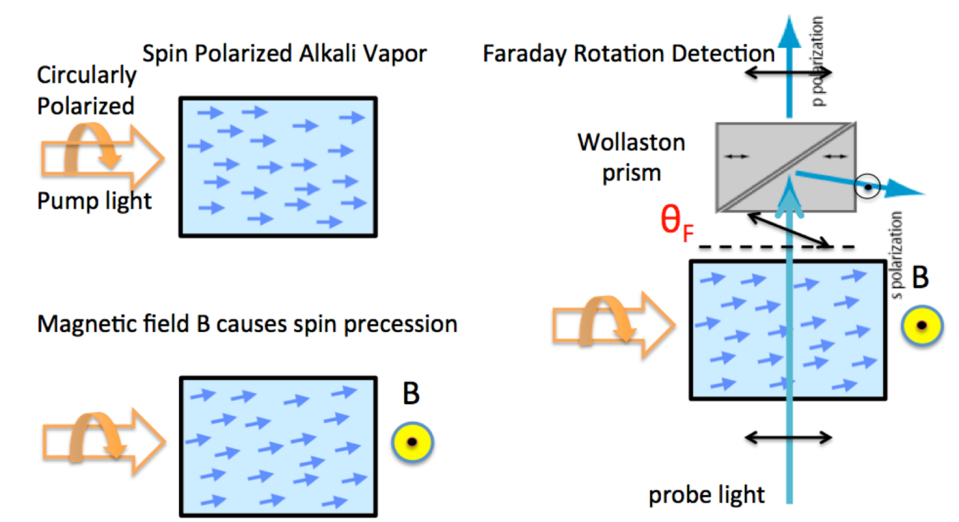

Figure 3 Principle of an optical atomic magnetometer. High dense alkali vapor is spin polarized by a resonant circularly polarized pumping light. External magnetic field will cause spins to precess, resulting in an orthogonal spin component. This component causes Faraday rotation of an orthogonal (off-resonant) probing light.

We have successfully developed a Sagnac interferometer near the resonance of Rb vapor's D1 line. As shown in the figure below A Rb vapor cell has been constructed with precision temperature control, which tunes the pressure, hence density of the vapor. The light source of the Sagnac interferometer can be precisely temperature controlled in order to tune its wavelength to the resonance wavelength of Rb vapor. The Sagnac interferometer is being put

together with the Rb vapor cell to make a magnetometer. A picture of the experimental setup can be found below.

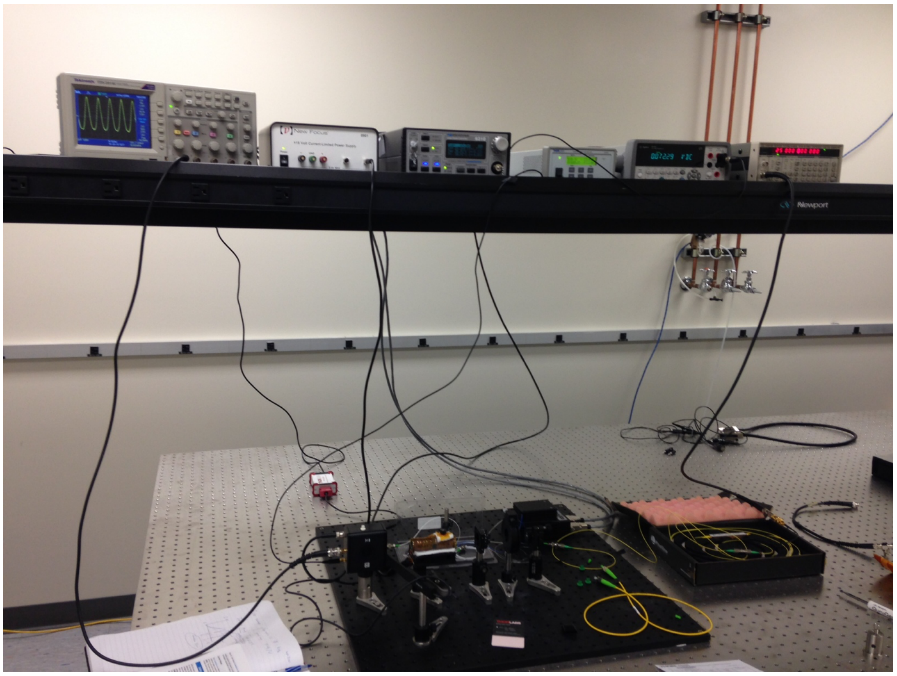

Figure 4 **Rb vapor cell coupled to the Sagnac interferometer**. The temperature controlled Rb vapor cell is on the left optical breadboard. The fiber Sagnac interferometer is on the right.

4) <u>other achievements. Include a discussion of stated goals not met.</u>

While the interferometer itself is performing well, we found it difficult to keep the wavelength of the pump laser tuned to the Rb vapor. The Rb vapor cell is temperature controlled to a precision of 0.01 C and optically pumped by a 780 nm laser. The Faraday signal from the optically pumped Rb vapor cell is measured by the Sagnac interferometer, whose temperature is controlled to maintain a steady wavelength.

In the following figure, the Y-axis is Faraday signal (log-scale) and the X-axis is time in seconds. It can be seen that the wavelength is not stable enough that the laser is coming in and off resonance every few seconds. Therefore the Faraday sensitivity is lost every few seconds when the laser is off-resonance.

Since the time-trace of this measured Faraday signal is step-like, we speculate that the instability of the laser wavelength is most likely due to mode-hopping of the light diode. If this is true, a mode-locked laser is needed to replace the laser diode we use in order to stably lock to the resonance of Rb vapor.

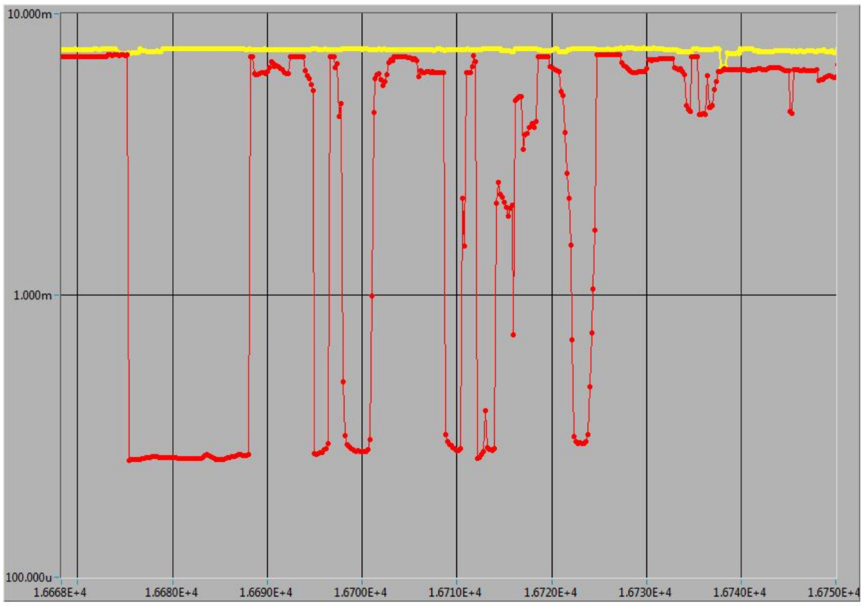

Figure 5 **Faraday noise of Rb vapor due to drifting of laser wavelength**. The Faraday signal from the optically pumped Rb vapor cell is measured by the 795 nm Sagnac interferometer, whose temperature is controlled to maintain a steady wavelength. The Y-axis is Faraday signal (log-scale) and the X-axis is time in seconds. It can be seen that the wavelength is not stable enough that the laser is coming in and off resonance every few seconds. Therefore the Faraday sensitivity is lost every few seconds when the laser is off-resonance.

Another possibility for the unexpected signal from the Rb vapor cell is possibly due to fluctuations in the environmental magnetic field. The Sagnac system was testing while operating in an unshielded environment. It is possible that nano-Tesla level of fluctuations in the magnetic field could result in the observed fluctuating signal. As some reading and investigation into commercial MEG systems, the PI realizes that all commercial MEG systems operate in magnetically shielded rooms usually constructed from mu-metal sheets. Quote for such a room is usually at $1 M level, which is beyond the budget of this grant. The PI is still trying to find a solution without such an expensive shielded room. Some ideas such as active magnetic cancelations coils have been considered but we haven't achieved satisfactory performance yet.

What opportunities for training and professional development has the project provided?

Via this project, the PI has taught graduate student Alex Stern how to work with lasers, fibers, optical modulators and other optical components. The PI has also taught undergraduate student Donald Trinh how to cleave and polish fibers and how to use Labview and Matlab software.

How were the results disseminated to communities of interest?

Some results of this project, namely the performance of the interferometer and its integration with a Rb vapor cell, have been included in the follow seminar talks given by the PI.

"What is a Sagnac interferometer and what can it do?", Physics colloquium at CSU long beach, March 9, 2015.

"Tuning ferromagnetism in ultra-thin perovskite films with a patternable capping layer", Physics seminar, UC Berkeley, April 13, 2015.

"What is a Sagnac interferometer and what can it do?", Physics seminar at UC Davis, May 7, 2015.

What do you plan to do during the next reporting period to accomplish the goals?

Nothing to Report.

IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

The constructed Sagnac fiber interferometer has demonstrated that 5 nrad level Faraday sensitivity can be achieved, even with an extended period of one week. Such recording-breaking Faraday sensitivity and stability opens new possibilities for precision magneto-optic measurements.

The pump laser diode is not stable enough to lock to the D2 line of the constructed Rb vapor cell for more than a second. This shows that a mode-locked laser is required for operating a Sagnac interferometer- Rb vapor cell system. Unfortunately, months have been

wasted into modifying and tuning the pump laser diode and the Rb vapor cell before the PI realized the necessity of a mode-locked laser, whose price tag is beyond the budget of this proposal.

What was the impact on other disciplines?

Nothing to Report.

What was the impact on technology transfer?

Nothing to Report.

What was the impact on society beyond science and technology?

Nothing to Report.

CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them

While the interferometer itself is performing well, we found it difficult to keep the wavelength of the pump laser tuned to the Rb vapor. The Rb vapor cell is temperature controlled to a precision of 0.01 C and optically pumped by a 780 nm laser. The Faraday signal from the optically pumped Rb vapor cell is measured by the Sagnac interferometer, whose temperature is controlled to maintain a steady wavelength. In Figure 5*, the Y-axis is Faraday signal (log-scale) and the X-axis is time in seconds. It can be seen that the wavelength is not stable enough that the laser is coming in and off resonance every few seconds. Therefore the Faraday sensitivity is lost every few seconds when the laser is off-resonance. Since the time-trace of this measured Faraday signal is step-like, we speculate that the instability of the laser wavelength is most likely due to mode-hopping of the light diode. If*

this is true, a mode-locked laser is needed to replace the laser diode we use in order to stably lock to the resonance of Rb vapor.

Unfortunately, months have been wasted into modifying and tuning the pump laser diode and the Rb vapor cell before the PI realized the necessity of a mode-locked laser, whose price tag is beyond the budget of this proposal.

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Changes that had a significant impact on expenditures

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to Report

PRODUCTS:

Publications, conference papers, and presentations

Journal publications.

Nothing to Report

Books or other non-periodical, one-time publications.

Nothing to Report

Other publications, conference papers, and presentations.

Some results of this project, namely the performance of the interferometer and its integration with a Rb vapor cell, have been included in the follow seminar talks given by the PI.

"What is a Sagnac interferometer and what can it do?", Physics colloquium at CSU long beach, March 9, 2015.

"Tuning ferromagnetism in ultra-thin perovskite films with a patternable capping layer", Physics seminar, UC Berkeley, April 13, 2015.

"What is a Sagnac interferometer and what can it do?", Physics seminar at UC Davis, May 7, 2015.

Website(s) or other Internet site(s)

Nothing to Report

Technologies or techniques

Nothing to Report

Inventions, patent applications, and/or licenses

Nothing to Report

Other Products

Nothing to Report

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

- *Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."*

***Example**:*

Name:	*Jing Xia*

Project Role:	*PI*
Researcher Identifier (e.g. ORCID ID):	*NA*
Nearest person month worked:	*2*
Contribution to Project:	*Mr. Xia has performed work in the area of design, construction, testing and data analysis of the instrument.*
Funding Support:	*NA*

Name:	*Alex Stern*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*NA*
Nearest person month worked:	*3*
Contribution to Project:	*Mr. Stern has performed work in the area of polishing fiber-optical components and assembling optical parts.*
Funding Support:	*NA*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report

What other organizations were involved as partners?

Nothing to Report

SPECIAL REPORTING REQUIREMENTS

Nothing to Report

APPENDICES:

Nothing to Report